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MORBID ANATOMY BEFORE AND AFTER MORGAGNI\*

*The Twenty-Third Middleton Goldsmith Lecture*

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IN 1761, Morgagni published his treatise,<sup>1</sup> "On the Seats and Causes of Diseases as investigated by Anatomy." Since then, Morgagni has frequently been called the "father of Pathologic Anatomy" and his monumental work its first textbook. Both claims are open to question. On the one hand, many records are available of necropsies performed for the explicit purpose of ascertaining the seats and causes of diseases which antedate the publication of Morgagni's masterwork;<sup>2, 3</sup> on the other hand, Schenck a Grafenberg's *Observationes*<sup>4</sup> and Bonetus' *Sepulchretum*,<sup>5</sup> likewise, had the same didactic aim of defining disease in terms of anatomic alteration. What, then, is the reason for celebrating the bicentennial anniversary of Morgagni's contribution to medicine? More than 200 years had preceded the publication of his book during

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which time anatomic examination had played an increasingly commanding role in the investigation of disease, and 200 years have passed since it has come off the printing press. History has placed Morgagni in a period almost equidistant from the inception of pathologic anatomy and its present phase. His work can be appraised looking backwards as well as forward from his time. His contribution can be regarded as the culmination of a gradual evolution of morbid anatomy and also as the foundation of a new concept of pathology as it developed in the 19th and 20th centuries.

Belief in the utility of morbid anatomy for medicine can be traced to the Hippocratic book on *Ancient Medicine*<sup>6</sup> where it is stated, "I am further convinced that it is necessary to know what sufferings come to a man from powers and what from shapes. I mean, roughly, by power an extreme strength of humor, by shapes, the various forms to be found among the parts of the body". It seems as if, historically, the belief existed *a priori* among physicians that anatomic investigations contribute to a clearer understanding of the causes of diseases. But such explorations were precluded by a powerful taboo against contact with the dead body which was lifted for a short period only during the reign of the Ptolemaic kings. When, during the 13th century, restrictions were relaxed for the purpose of anatomical teaching, clinical autopsies were also soon performed. But the early reports did not clarify obscure clinical problems by the demonstration of relevant organ lesions. The anatomical findings were sometimes unequivocally described, but correlated with ill-defined clinical syndromes without empirical corroboration, while in other instances the reported anatomic alterations could not adequately account for the course of the disease. For example, in the case of Tornius,<sup>7</sup> symptoms of fever, discoloration of the face and dyspnea were interpreted according to Galen and Avicenna as evidence of obstruction of the liver and abdominal veins. The autopsy disclosed multiple ulcerations of the liver, most probably pylephlebitic liver abscesses in today's terminology, in addition to obliterating plugs in the portal and inferior caval veins. This satisfied Tornius to make the final comment: "So I was assured on seeing the cholic veins that there was an obstruction, as I had suspected." On the other hand, Benivieni<sup>8</sup> does not account for well-defined clinical symptoms in terms of unequivocal anatomical alterations, except in cases where such correlation is obvious. This unsophisticated attitude is illustrated in his description of an intes-

tinal obstruction by a callous mass, evidently a carcinoma. His comment is: "This, however, I had suspected even in her lifetime, seeing that she had struggled against something hard that pressed on her bowels." In subsequent years, many more observations were recorded in which the leading clinical symptoms were determined by mechanical factors disclosed at autopsy. Fernel<sup>9</sup> in 1567 summarized such situations in the following paragraph: "Similar to obstruction is constriction and narrowing of the intestine. This may be produced by the actions of things ingested, whether foods, as bad bryony, or astringent drenches, also by tumour of the mesentery or by the viscera pressing on the intestines and this is extremely common. It also happens from enterocele when the intestine comes down into the scrotum and is constricted by it as by a loop. Each of these ought to be perceptible of itself and not indirectly." Bonetus<sup>10</sup> *Sepulchretum* is replete with autopsy records in which morbid symptoms affecting various regions of the human body are unequivocally correlated with anatomic alterations acting as mechanical impediments. All the great physicians of the two centuries preceding the publication of Morgagni's work opened the bodies of their deceased patients, anticipating to account for the clinical symptoms as a result of perceptible anatomic changes. It was a sort of common sense pathology which even those whose fundamental idea of the nature of health and disease was far from materialistic did not reject. Thus, van Helmont<sup>10</sup> refers to many necropsies which he performed on hydropic patients in order to ascertain whether the liver was affected or not. Even Sydenham,<sup>11</sup> who saw the possibility of progress in medicine only in exact bedside observation, did not altogether disapprove of autopsies but conceded their limited usefulness for the medical practitioner. Only John Locke<sup>12</sup> rejected anatomy as a tool of medical investigation. With the advance of rational physiology since Harvey, clinical symptoms could better be interpreted in terms of disturbance of organ functions and consequently more appropriately correlated with observations at the autopsy table. Thus, not only diagnostic medicine was enhanced but also new problems proposed for physiology. Edematous and cold extremities were correctly interpreted by Brunner<sup>13</sup> in his discussion of the autopsy of his father-in-law, Johann Jacob Wepfer, as the result of a failing greater circulation and not of a loss of innate heat. That cyanosis and dyspnea are due to stagnation of the pulmonary circulation was pointed out by Vieussens and Albertini.<sup>14, 15</sup> That apoplexy is

caused by rupture of cerebral arteries was disclosed by Wepfer.<sup>16</sup> Sudden death due to occlusion of cardiac arteries was suggested by Bartholin.<sup>17</sup> Gangrene of the extremities was accounted for by ossification, and narrowing of the arteries by Evelyn and Cowper in 1702<sup>18</sup> and by Naish<sup>19</sup> in 1721. The association of polyuria with contraction of the kidneys was recognized by Wepfer<sup>20</sup> 150 years before Bright and Christison and this puzzling problem of renal pathology first exposed in terms of anatomic localization.<sup>20a</sup>

In 1679, Théophile Bonet assembled from the literature 3,000 cases in which clinical data had been reported with corresponding autopsy findings and complemented with explanatory remarks. Indeed, this collection shows the notable achievements of morbid anatomy over the past two centuries, but it also illustrates that its localizing principle had failed so far to account for a multitude of diseases. It could answer some of the problems of a crude mechanistic doctrine of health and disease as proposed by Descartes, but left unanswered the ultimate questions of the factors which regulate normal and abnormal life. For more than 2,000 years a speculative humoral pathology had satisfied the curiosity of the medical profession; the emerging modern basic sciences of physics and chemistry could easier be assimilated to this doctrine than aligned with an unsophisticated concept based on the as yet inadequate empiricism of morbid anatomy. Therefore, humoralism reinforced by iatromechanics and iatrochemistry could successfully compete with solidism proposed by morbid anatomic investigations. In fact, humoral speculations could be used for the explanation of anatomic organ alteration as evidenced by the writings of Malpighi<sup>21</sup> and Lancisi.<sup>22</sup> This was the intellectual climate of medical theory at the beginning of the 18th century when Morgagni entered the arena. The soundness of the principle of interpreting by anatomy the symptoms of diseases was established, but information was still fragmentary and not adequately collected and catalogued. Bedside and autopsy observation had still to be developed to a higher accuracy and validity of correlation critically examined. To assemble all the pertinent clinical and anatomic facts and to recognize their interrelations required a man of broadest experience and an exceptionally keen mind. To complement one's own observations with those accumulated over a period of 200 years in the literature of Europe called for a man of rare scholarship. And finally, it required the unshakable conviction that this work had to be done. Morgagni

brought all these qualifications to the task. He had been schooled by his teachers, Valsalva and Albertini, in the strict anatomical tradition of Malpighi, whose scientific grandson he proudly pronounced himself. It is generally maintained that Morgagni was primarily a morbid anatomist and his training and subsequent work in anatomy lend credence to this belief. But Jarcho,<sup>23</sup> in a penetrating study, challenges this opinion and shows from his writings that his interests were by no means strictly morphological. A perusal of the "Seats" reveals that Morgagni paid at least equal attention to the description of bedside symptoms as to autopsy observations of organ alteration. Morgagni's practical orientation directed him toward advancing clinical diagnosis, not as an end but as a means to the ultimate purpose of alleviation and cure of disease. This aim is well illustrated by his endeavor to discover pathognomonic features by persistent correlation of clinical symptoms with anatomical alterations. His attitude is revealed in many parts of his books and clearly expressed in his prefatorial letter to Johann Friedrich Schreiber.

He had at his disposal the material of the Hospital of St. Francesco in Padua, the records left to him by his teacher Valsalva and, last but not least, the observations of preceding generations. For nearly 60 years, he assembled data before he completed his monumental work. He had gained his reputation as a superb anatomist by his previous treatises, the *Animadversiones* and the *Epistolae Anatomicae*, which made him the undisputed leading anatomist of Europe. In 1708, he was elected a member of the Leopoldino Carolino Academy in Germany of which he became a deputy president in 1732; in the subsequent decades, all the national scientific societies of Europe selected him for inclusion in their ranks. In 1716, Boerhaave offered him without success the Chair of Anatomy at the University of Leyden, and Senac, in 1749, referred to him as the illustrious author of a forthcoming encyclopedia of anatomy. But anatomic investigations were not the ultimate aim for Morgagni, not even if pursued for elucidating the actual functions of organs; they were only means to the end of advancing the theory of medicine and of its practice. And so he wrote these books "concerned with the history of pathologists more than with anatomists", as he stated in his letter to Senac, prefatorial to the third book. But his vista of pathology is limited, though by intent. He was aware of those authors, who "affirmed that the causes of health as well as of most maladies are inaccessible to the senses, since they rest in hidden forms of invisible

particles, in their connections and movements and its forces which control these movements and connections". But he is not concerned with these hidden reasons "because it does not follow that the effects of these causes necessarily also escape our senses; for they affect perceptible parts and the abnormal alteration, which we discern in them, are the manifest internal causes of very many diseases". With this statement Morgagni unequivocally states the positivistic aim of morphologic investigation for the advance of medicine and refrains from hypothesis and ratiocination. He accepts only observation and description and his goal is a Natural History of Diseases, in the sense of Bacon, in which symptoms are correlated with anatomic alterations and these data reciprocally indexed. These indexes should serve, as he writes in the preface: "So that if any physician observe a singular or any other symptom in a patient and desire to know what internal injury is wont to correspond to that symptom; or if any anatomist find any particular morbid appearance in the dissection of a body and should wish to know what symptom has preceded an injury of this kind in other bodies; the physician, by inspecting the first of the indexes, the anatomist, by inspecting the second, will immediately find the observation which contains both (if both have been observed by us)."

Morgagni's fundamental objective was that of exact empiricism. He had the vision of a catalogue in which all the disease phenomena were critically collected and cross-indexed. His aims can be compared with those of Diderot, when he conceived his plan of an encyclopedia. He was aware of the magnitude of his project and invited the cooperation of all physicians and anatomists. (Letter to Frederick Meckel.) He foresaw that future generations would still be engaged in the task of providing the medical profession with a complete register of integrated clinical and anatomical data. He tried to caution future investigators of the pitfalls of anatomic observations and pointed to organ alterations occurring in the moribund patient and even after death. Such changes had often been misinterpreted in the past, as, for instance, postmortem coagula had been considered polypi of the heart. He cautioned that a correlation between anatomical findings and clinical symptoms must be validated by an adequate number of observations, the statistical principle already stressed by Francis Glisson<sup>24</sup> 100 years before. He emphasized the importance of listing age, sex, marital status, occupation and climatic conditions affecting the patient, and did not neglect to point to previous

diseases and hereditary factors which should be looked for. Thus, he emerges from his writings as the great teacher, a vocation which was most precious to his heart, a sentiment he unequivocally expressed in his letters to Senac and Schreiber. The didactic orientation transpires throughout his five books and is expressly stated in the prefatory pages. The dynamism of teaching elicits, as a necessary corollary, a desire for more learning. It is the combination of these two forces in Morgagni which explains how morbid anatomy, as sponsored by him, did not become a mere branch or tool of medicine but its discipline, and that it could grow harmoniously beyond the peak it had reached with him.

Morgagni's books were received by the medical world with the greatest respect. *The Göttingische Gelehrte Anzeigen* of July 25th, 1763, wrote that it would be impossible to abstract his "important and for all true physicians indispensable work". Haller<sup>25</sup> referred to them as most significant and important and praised Morgagni for having been an outstanding anatomist in his youth and for having reached even higher eminence in his advanced years by his most important contribution to the practice of medicine and morbid anatomy. The books were translated into English in 1769, into German in 1774. They were followed in due course by similar collections of clinical-anatomic correlations, such as those of Lieutaud<sup>26</sup> and of Sandifort.<sup>27</sup>

It had been stressed by Morgagni that a full comprehension of disease demanded its localization in order to define it. An awareness of this postulate emerges in the regretful remark of Heberden<sup>28</sup> in his first publication on angina pectoris when he writes of his inability to perform an autopsy on any one of his patients. This example well illustrates that Morgagni's contemporaries were cognizant of the value of post-mortem examination, but not convinced of its indispensability for a deeper understanding of disease. However, the nature of this "disorder of the breast" began to be clarified only when Jenner and Parry<sup>29</sup> established its correlation with coronary artery ossification in 1799. It is at the turn of the century that the impact of Morgagni's thesis gained momentum. It does not detract from his glory if it is reiterated here that the idea of clinical-anatomical correlation did not originate with him, but he advanced it with his authority and his monumental contribution. One must not fail to mention that Boerhaave, in Leyden, had already made obligatory post-mortem examinations on the patients whom he had presented to his students in his clinical demonstrations.

It was under the influence of his disciples, Van Swieten and De Haen, that the same practice was introduced in the government hospitals in Vienna in the middle of the 18th century, and it was in Vienna where a new idea was born which was to vitalize the principle of congruence of observations in the living and in the dead which Morgagni had advocated so persuasively and codified at the end of his life. Leopold Auenbrugger's slim *Inventum Novum*<sup>30</sup> appeared in the same year as Morgagni's voluminous work. Here the novel idea was first proposed to make morbid lesions of the chest perceptible by percussion. Obviously, this brilliant discovery could be fully utilized only if the anatomic rationale had already taken firm roots in medicine. It had not, and it required nearly 50 years until Auenbrugger's genius found full recognition, thanks to the discernment and generosity of Corvisart. With this ingenious clinical technique new diagnostic symptoms were added to the conventional criteria of medical examination, aiding the ultimate aim of an anatomic diagnosis of organ alterations in the living. That this was the aim was succinctly expressed by Corvisart<sup>31</sup> in the preface to his essay on cardiac diseases, in which he recommended the preparation of "a book analogous to that of Morgagni but the converse of it"; it would be titled, "On the Seats and Causes of Diseases, Investigated by Diagnostic Signs and Confirmed by Autopsy". "But," he added, "for such a work we would need at least a second Morgagni." Corvisart's prophecy has come true. It was advanced by Laennec's discovery of auscultation, and was carried to unexpected heights by roentgenology and the diverse modern methods of biopsy in the literal meaning of the word. It still shows its value and vitality in the clinical-pathological conferences of today. The history of medicine of the first half of the 19th century has proven Corvisart right. But it required more than a book to consolidate the new rational medicine based on morbid anatomy. It developed all over Europe but reached its height in France under the inspiration of Pinel, Bichat and Corvisart; in England, of John Hunter. The achievements of these schools of medicine with primary anatomic orientation within the span of the first decades of the century cannot be given in detail. But reference should be made to the discovery of the characteristic intestinal lesions in the obscure putrid, ataxic or typhoid fever by Petit and Serre in 1813,<sup>32</sup> because it brought into sharp focus the basic inadequacy of single-minded clinical-anatomic correlation. More than 50 years before, Senac and Morgagni



had remarked on the absence of obvious anatomic alterations in the group of malignant fevers to account for the leading symptoms (Morgagni's letter to Senac<sup>33</sup>). Now the new observations had disclosed unequivocal intestinal lesions; but how could they be correlated with the equally striking and variegated morbid phenomena during the life of the patients? It is true that Petit and Serre had recognized that the initial symptoms of the malady pointed to an affection of the intestines, an observation agreed upon by all subsequent observers; but how could all the other conspicuous symptoms, especially the severe cerebral affection and the prostration be explained? This uncertainty is revealed by the remark of Cruveilhier<sup>34</sup> who was familiar with the disease both clinically and anatomically. Referring to the entero-mesenteric fever of Petit and Serre, he raises the question whether the organic alterations reflect the principal disease, or a complication, or whether they are an effect of the fever. He even questions the specificity of the intestinal lesions which he believes to occur in several other maladies, among which he mentions mainly pulmonary phthisis. This, of course, showed only diagnostic inadequacy, which was soon corrected, as can be recognized in Richard Bright's classical plates<sup>35</sup> which clearly illustrate the differences between tuberculosis and typhoid ulcerations. Bretonneau<sup>36</sup> in 1829 unequivocally maintained that the disease, which he called *DOITHINÉNERIE*, is accompanied by intestinal eruption but not caused by it, "because one cannot, without grave error, attribute the morbid phenomena characteristic of it to an intestinal inflammation". These were serious challenges of the universal validity of Morgagni's fundamental assumption that anatomical alterations were the proximate causes of diseases. They questioned the wisdom of his attitude of refraining from concern with the hidden causes of disease. They indicated that morbid anatomy could not remain satisfied with merely demonstrating a parallelism between clinical and morphologic phenomena of disease, but that it had to aim at a comprehension of the nature of the anatomic lesions. If pathology is that aspect of medicine which is concerned with the cause of disease and the mechanisms by which it is provoked, then, if morbid anatomy is to be auxiliary to pathology, it must abandon its static taxonomic position and has to inquire into the reasons for structural aberration; in other words, it has to develop into anatomic pathology. The findings of Petit and Serre and of their successors offered a key which opened a new approach for a better comprehension of dis-

ease through morbid anatomy. Their exact observations had disclosed that the intestinal lesions of typhoid varied with the duration of the illness. This indicated that the structural alterations were dependent on a biological evolution and therefore had to be regarded as the product of a morbid process. This concept vitalized the interpretation of the static structural anomaly and prevented morbid anatomy from becoming a mere appendix of diagnostic medicine. It oriented Bayle<sup>37</sup> and Laennec<sup>38</sup> in their investigations of pulmonary tuberculosis; it led Abercrombie<sup>39</sup> and Rostan<sup>40</sup> to recognize encephalomalacia as the result of vascular occlusion; it transpired in Bright's discussion of his new disease. The importance was fully recognized by Lobstein, but it became the lode-star for Rokitansky and Virchow and it still dominates the philosophy of our discipline today. While a chronicle of pathologic anatomic discoveries seems to indicate that the concept of the morbid process was advanced in the 19th century only, it has to be affirmed that it can already be recognized in the lectures on surgery of John Hunter<sup>41</sup> and his works which were published after his death. He was led to the principle by his observations as a surgeon and guided by it in his studies and experiments on inflammation. Matthew Baillie,<sup>42</sup> his nephew and disciple, grasped the importance of the pathogenetic principle for the advance of morbid anatomy when he wrote in the preface to his textbook that "the object of this work is, to explain the changes of structure arising from morbid actions". But he realized that the observational material was still inadequate because he continued, "it is very much to be regretted that the knowledge of structure does not certainly lead to the knowledge of morbid actions although the one is the effect of the other". He was aware of the difficulty of gaining knowledge, "because", he said, "morbid actions are going on in the minute parts of an animal body excluded from observation". This assertion sounds like that of John Locke,<sup>12</sup> who had maintained about 100 years before that "nature performs her operations in the body by parts so minute and insensible that I think nobody will ever hope or pretend even by the assistance of glasses to come to a sight of them". Yet, Baillie did not share Locke's pessimism because he ended his considerations with the affirmation that, "examination of morbid structure seems to me to be one of the most probable means of throwing light on it". And the development of the next 50 years proved him right.

But the historian has to caution himself not to attribute conceptual

advances in medicine to selected observations or to the genius of individual investigators. The dynamism which began to pervade the studies of morbid anatomists in the first decades of the 19th century originated in the conscious efforts of physiology to analyze experimentally the actions which take place within the parts of the body. Not that the idea of a function of organs was alien to preceding generations of physicians. Galen had written books on the subject, and the great anatomists of the 16th and 17th centuries had paid equal attention to structure and function. To quote only Glisson<sup>43</sup> among them: "Nobody is interested in the manual dissection of cadavers if it does not bring light to the comprehension of the living." But the well-spring of action was not observed but left to speculation, be it that of an *Archaeus*, an *Anima*, or of the less mystical but not better comprehended forces invoked by iatromechanics and iatrochemists. The first determined effort was made by Albrecht von Haller to investigate the actions of parts of the body in reference to two phenomena which he observed by experiments. These were the elicitation of pain and of contraction. In his essay<sup>44</sup> on the "sensible and irritable parts of the human body" he concluded that the vital phenomena are determined by a particular organization of the respective tissues, reacting to stimuli, an idea which was fully developed by Virchow in his cellular pathology. I shall not enter into a discussion of the far-reaching and erroneous conclusions which were drawn from Haller's strictly physiologic observations as regards an explanation of the nature of disease, such as, the neuristic theory of Cullen and particularly John Brown's irritability doctrine. But I should like to point to the connection between Haller's fundamental observation of the localization of vital phenomena within well defined anatomic structures and the ideas of Bichat.

The assumption that the function of organs depends on a special vital force and not on mechanical factors, an idea contrary to that of Boerhaave, was first expressed by Théophile Bordeu<sup>45</sup> of Montpellier in the same year in which Haller published his essay. Bordeu, 16 years later,<sup>46</sup> was again the first who pointed to the cellular tissue, today's connective tissue, as the seat of many diseases. Both suppositions are combined in Bichat's doctrine. It is obviously impossible to give in this address an abstract of Bichat's observations which culminated in his *General Anatomy*, his essay on the membranes and on life and death. But it might be permitted to quote two sentences which succinctly sum-

marize his beliefs.<sup>47</sup> They could be duplicated by many more. "I believe that the more one will observe diseases and open the cadavers the more one will be convinced of the necessity of considering local diseases not from the aspect of the complex organs but from that of the individual tissues." And his physiological concept he expressed with the following sentence: "To apply the physical sciences to physiology means to explain the phenomena of living with the laws of dead bodies. Leave affinity to Chemistry, to Physics its elasticity and gravity, to physiology pertains only sensibility and contractility." Bichat's definition of tissues, and the idea of localization of morbid processes in them and not in complex organs, was generally accepted as evidenced by Hodgkin's lectures on the morbid anatomy of the serous and mucous membranes.<sup>48</sup> How far Bichat's cumbersome method of tissue investigation influenced the observations of pathologic anatomy is not easily ascertained, because the microscope was soon introduced for the study of finer details.\* His importance for the advance of the discipline was undoubtedly due to the enthusiasm which he kindled among those with whom he came in contact. Dupuytren, Laennec and Bayle were his direct pupils, and through these, new future generations were instructed in pathologic anatomy, among them Cruveilhier and Louis in France, Hodgkin and Carswell in England and Gerhard in this country. Bichat's doctrine of life and his rejection of physical or chemical explanation of phenomena of the living organisms soon met energetic opposition. It grew when the advances of organic chemistry showed that the assumption of a difference between organic and inorganic matter was not tenable. The idea of vital tissue qualities and forces is no more acceptable today, but it played an important role in the development of biology, because it encouraged the incessant efforts of the exact sciences to refute it and to substitute physico-chemical laws for the ill-defined actions of a hypothetical force.

Notwithstanding these cogent objections, both doctrines of Bichat equally contributed to the evolution of pathologic anatomy in the subsequent decades. His morphologic proposition of localizing the anatomic alterations in the tissues instead of the complex organs was by itself a refinement only of Morgagni's original thesis. Linked, however, with the postulation of a force, regulating the life of the tissues, the idea was

\* His immediate pupils did not engage in a study of the tissues but remained interested in the lesions of the whole organs and developed pathologic anatomy in such a manner that it became known under the name "organicism".

introduced into the study of structure of causal determinism, an idea from which Morgagni had kept aloof intentionally. To the assertion that the causes of health as well as of most maladies are inaccessible to the senses, he had replied with a skeptical "even if true" in his letter to Senac. Forty years later, the question could no longer be sidestepped, if morbid anatomy was to contribute to general pathology, the fundamental theory of medicine. It was, however, scientific search for the internal causes of tissue changes which was to be launched only in the years to come; neither postulation nor speculation could bring about the transformation of Morgagni's unsophisticated concept. Interestingly, most morbid anatomists of the first third of the 19th Century were not aware of the crisis in which their discipline would find itself in the not too distant future. In fact, that period witnessed some of the most important contributions to medicine yet achieved by the classical correlative principle of Morgagni, such as Laennec's monumental work on *Diseases of the Chest*,<sup>38</sup> the discoveries of Bright<sup>35</sup> and Hodgkin,<sup>49</sup> in addition to those already mentioned previously. Medicine in France, England and in Germany under Lucas Schoenlein following the decline of NATURPHILOSOPHIE was conducted mainly along diagnostic lines with morbid anatomy as the sole guide. It is obvious that such an orientation was not disposed to advance the ultimate aim of curative medicine which could only be established upon a sound scientific theory of general pathology.

Karl von Rokitansky and Rudolf Virchow are commonly regarded as the originators of a new pathologic anatomy. But again, history reminds us that new concepts in medicine do not arise *de novo* in the minds of single individuals; they are the results of a slow evolution which is only catalyzed by the clarity and perseverance of the chosen few. The impasse in which morbid anatomy found itself in the thirties of the 19th century was recognized by Lobstein in France and Johannes Mueller in Germany, and we can trace to their writings the immediate stimulus for modern anatomic pathology. In the preface to his textbook,<sup>50</sup> published between 1829 and 1833, Lobstein, the worthy descendant of Bichat, gave an outline for the organization of pathologic anatomy. Of his points I shall select a few because they represent a blueprint for the work of the future. It is founded upon exact description of the anatomic lesions according to position, shape, volume and internal structure of the affected organ and its relation to other anatomic systems with which it is connected in more or less sympathy, in

plain language, concomitant lesions of other organs. Under the term, "pathogenesis", first used by him in pathologic anatomy, Lobstein embraces the investigation of all questions regarding origin, formation and evolution of the organ disease. The final but not less important objective of pathologic anatomy is to correlate the organic alteration with the morbid phenomena observed during life. This is, of course, the classical precept of Morgagni. But Lobstein demanded a more penetrating analysis of the phenomena in order to determine to what degree they are dependent on the anatomic lesions. Such an inquiry should aim at a distinction of the original symptoms which pertain to the immediate affection of the vital force from those which are direct consequences of the manifest alterations of the tissues. Lobstein's principles of pathologic anatomic investigations have been faithfully followed by Rokitsky who in his autobiography acknowledged his indebtedness to him. If Lobstein said that "the physician does not want to concern himself with the dead organ but with that which lives and acts", Rokitsky carried out this objective because he taught, as Klebs<sup>51</sup> expressed it, "to think anatomically at the bedside and to weave at the autopsy table the individual phases of the morbid process into the pattern of the clinical progress". This was the program of which Rokitsky spoke<sup>52</sup> to his students at his first lecture as full professor and to which he turned 30 years later in his last lecture<sup>53</sup> when he said: "I have pursued Pathologic Anatomy as a science aiming at fertilizing clinical Medicine." But Lobstein's influence went beyond stimulating Rokitsky's endeavor of promoting conventional morbid anatomy. The recommended separation of the aims of correlation was an equally important clue for Rokitsky's interpretation of autopsy findings. The symptoms pertaining to affection of vital forces could not be expected to correspond to local changes of organs, but rather to those of the all-pervasive humors of the body, particularly the blood. It seems to me that his crisis doctrine derived from that assumption. It is true that this speculation collapsed under the harsh critique of Virchow. But Rokitsky had realized that investigations of the whole blood could not be adequately carried out with the methods of morphology but demanded profound chemical research. And so the ill-fated "Krisis Doctrine" gave birth to a scientific exploration of the altered constitution of the blood, and Rokitsky conceived of a discipline devoted to the chemical aspects of pathologic inquiry, as he affirmed in his first lecture. This inspiration came to its

fulfillment in 1862 when the new Institute of Pathologic Anatomy and Pathologic Chemistry was opened in Vienna.

Historians have always been aware of the decisive influence Johannes Mueller had on the life work of Rudolf Virchow, and he has acknowledged it in his memorial address of this great scientist. But it might not be amiss to hear what Mueller had to say about the crisis in pathologic anatomy and how he proposed to meet it. In 1834, he wrote,<sup>54</sup> "Pathologic Anatomy continues to offer us a large amount of observations but their comprehension advances all too slowly. Among the obstacles of a further evolution one has to blame principally the unscientific casuistic trend with which it is pursued. It is carried out only for correction of diagnosis and not for the aim of advancing Pathology." And he points to the method by which this could be accomplished. "If anything should come out of the study of Pathologic Anatomy, physicians must not limit themselves to autopsy reports; the structure of the altered tissues must be investigated which requires adequate anatomic and physiologic experience". Johannes Mueller started this program with his study, "On the Finer Structure of the Forms of Neoplasms", but it was Virchow who completed it with his cellular pathology. Virchow is commonly regarded as the father of cellular pathology but not as the creator of the cell theory. This is correct, and it should be added that Theodore Schwann had already indicated that his cellular theory of the formation of normal tissues applied also to a great variety of pathologic organizations. Neither should it be ignored that Karl Remak preceded Virchow in the recognition that Schwann's original idea of cell formation from a formless blastema was not tenable and that he, prior to Virchow's early pronouncements of cellular pathology, published an article<sup>55</sup> in which he demonstrated that the principle of successive cell generation applies also to neoplasms. It might seem, therefore, that Arnold Rich<sup>56</sup> in 1926 was justified when he stated that "it required not much imagination to apply the microscope to the examination of morbid products". But Virchow's histopathology is not a mere refinement of Morgagni's thesis to recognize the perceptible organ changes, an advance of Morgagni's anatomy, thanks to technological progress. What we owe him is a new scientific approach to the comprehension of the nature of disease through analysis of structure. Through him the microscope became a reformatory instrument, not a mere diagnostic tool; in short, he is the creator of anatomic pathology, the morphologic discipline

which inquires not so much into the cause of disease as into the mechanisms by which it is provoked. I believe we can accept this restricted definition for our times. But in the years of Virchow's greatest triumph cellular pathology was acclaimed as the essence of pathology in general. This claim led to a crisis which came into the open at a meeting of the German Naturalists and Physicians in 1877. In an address entitled, "The Transformation of Medical Concepts in the Last Three Decades", Edwin Klebs,<sup>51</sup> a former assistant of Virchow, spoke respectfully but critically about the inadequacy of cellular pathology as a general theory of diseases. It was the rejection by Virchow of the recent achievements of bacteriology which prompted Klebs to refer to cellular pathology as "a theory which does not provide clarification of the causal conditions of diseases". The judgment of history has endorsed Klebs. But it might be informative to dwell on the question, how was it possible that the great Virchow should have been so blind as not to recognize the transcendental significance of the discoveries of Pasteur and Koch? A statement of Klebs might help to bring the issue into focus. I refer to the sentence in which he speaks of an "extreme doctrine which regards all morbid processes as purely internal events and completely neglects the importance of external factors which provoke the diseases". This doctrine was the result of Virchow's deliberate preoccupation with the comprehension of vital phenomena by concentrating upon their manifestations within the cells of the body. He was fully aware that an ultimate theory of disease must derive from coordinated investigations at the bedside and at the autopsy table and must include an inquiry into the morbid factors tested by experiment. This was his original program which he had outlined in 1845,<sup>57</sup> to which he adhered to the end of his life, and the execution of which he tried to advance by his research and by numerous inspiring lead articles in his *Archiv* and other publications. It was this great vision of universality which made him the leader of German Medicine and for which he was recognized all over the world. But for his own contribution in this grand scheme of endeavor he selected investigations of cell structure, in order to comprehend the phenomena of life. Truly, not structure in a narrow morphologic sense; for that we have him as a witness when he maintained that the alteration of the cell which he visualized in his mind need not be anatomic: "Can it not be chemical?" he asked.<sup>58</sup> Nine years later,\* he

\* At a meeting in Stettin in 1863.



gave a blueprint of his aims for analytical pathology: "When I called attention to the cell I intended to urge the individual investigators to identify precisely the events within the cells, what takes place within these smallest elementary organisms; and it was self-evident that this precise identification could not be anything else than to find the physical and chemical foundation upon which rest the vital phenomena."<sup>59</sup> This sounds like an up-to-date manifesto which should satisfy the most modern cell biologist, and it may hearten the anatomic pathologist daunted by the spectacular advances of today's biochemists and biophysicists. We must be grateful to Klebs for his criticism of cellular pathology, because it gave Virchow the opportunity<sup>60</sup> of clarifying his position and that of anatomic pathology. Just like Morgagni, who refrained from searching out the hidden causes of diseases and was satisfied with investigating their perceptible effects upon the organs of the body, Virchow did not concentrate upon identification of external factors which provoke the morbid state. But he was fully aware of their significance and expressed it repeatedly in subsequent articles, for instance, when he "calls attention to the fact that morphology represents only one aspect of biology and that beyond the confines of morphology there is a large area of mechanical and chemical events whose investigations require methods other than those morphology can supply". This statement reflects a balanced estimate of the potential of structural research. That Virchow did not unreservedly accept the microbic theory of infectious diseases can be accounted for by the extravagant and not always fully proven claims which some of the early enthusiastic followers had made, to whom he refers in his answer to Klebs. Another reason was his apprehension that the concept of disease as a living entity, held by German *NATURPHILOSOPHIE* only a generation before, could be revitalized by speculative minds. He had fought these erroneous ontological notions in the beginning of his career and was sensitized to them. He did not realize that these ghosts had been banned forever.

Klebs' courageous but restrained critique of cellular pathology was matched by Virchow's conciliatory response. When Klebs expressed the hope "that an agreement could be reached in the interest of the problems which cannot be solved by a single person", Virchow referred to misunderstandings which can be clarified, and disclaimed "the pretense that cellular pathology was meant to be a general Pathology".

The dignified controversy cleared the air and opened the road for auspicious cooperation of all sincere students of disease. The following generations of pathologic anatomists joined the ranks of those who had revolted against an all too narrow limitation of pathologic research and contributed to the rapid development of bacteriology and immunology, without abandoning their prime interest in anatomic pathology.\* It became evident that exclusiveness of purpose was harmful for the advance toward the common goal, general pathology, as the integrated comprehension of all the factors responsible for the morbid state. The ever-increasing scope of experiences in this endeavor is determined by an ever-increasing variety of methodology. We are sometimes losing sight of the unifying aim. Accelerated specialization and petty jealousies between the groups harm the harmonious development of sound teaching and research and endanger the whole structure of medical education. Respect for the common past will counteract these harmful influences which otherwise might threaten the vitality of Pathology in its universal meaning as that aspect of Medicine which is concerned with the cause of disease and the mechanisms by which it is provoked.

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\* The history of Experimental Pathology will be reviewed in a separate article.

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